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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,589	06/08/2000	Katherine A. High	018743/0276324	1864

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/589,589	HIGH ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-8,10,12-21,23-25,28,29 and 31-42* is/are pending in the application.

4a) Of the above claim(s) *42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-8,10,12-21,23-25,28,29,31-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Non-Final Rejection

Claims 1-4, 6-8, 10, 12-21, 23-25, 28, 29, and 31-42 are pending.

Applicant's traversal, the cancellation of claim 30 and the addition of claims 41 and 42 in paper filed on 1/26/06 is acknowledged and considered.

Election/Restrictions

The non-elected species in claims 16, 19, 32 and 37 remain and claim 42 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/15/01.

Claim Objections

Claims 8 and 17 are objected to because of the following informalities:

A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

If and when claims 8 and 17 are in condition for allowance they will have to renumbered.

Claims 1-4, 6-8, 10, 12, 13, 15-21, 23-25, 28, 29, 40 and 41 are objected to because of the following informalities: the phrase "blood coagulation protein being the same species as said mammal" is grammatically improper. Suggest inserting -- from -- after the term being.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 12-18, 21, 23, 25, 29, 31-36, 39, and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Conti-Fine (US 6,929,796). Conti-Fine teaches a method of inhibiting or preventing inhibitory antibodies to Factor IX in a subject (e.g., humans) comprising administering an immunosuppressive agent, wherein the Factor IX is delivered via gene therapy to the subject (abstract and columns 3-7, 14-15, and 30). The gene therapy to the subject (e.g., human) comprising administering viral vector comprising Factor IX being from the same species as the subject (columns 4-6 and 14-15). The viral vector can be an adeno associated viral vector (columns 6, 15, and 27). The subject has hemophilia B, wherein the subject does not produce Factor IX (columns 6 and 15).

Applicant's arguments with respect to claims 12-18, 21, 23, 25, 29, 31-36, 39, and 40 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-8, 10, 12-21, 23-25, 28, 29, and 31-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilson et al. (US 6,251,957) taken with Conti-Fine (US 6,929,796). A method of inhibiting in a mammal formation of neutralizing antibodies directed against a virus comprising the step of co-administering to said mammal said virus and a combination of immune modulators which inhibits neutralizing antibodies against said virus, wherein the combination of immune modulators consists of cyclophosphamide and an anti-CD4 monoclonal antibody (columns 25-26). Wilson teaches a gene therapy method comprising co-administering with a viral vector comprising a heterologous nucleotide sequence and an immunosuppressive agent to a human (column 2, lines 35-52, column 4, lines 20-34 and column 25-26). Wilson teaches that the viral vector can be AAV (column 26). Wilson teaches that an immune response can be the

product of the transgene when that transgene expresses a protein that is foreign to the treated host (column 1). Wilson teaches that the immunosuppressive agent may be administered prior to or concurrently with the recombinant viral vector (column 2, lines 45-49). However, Wilson does not specifically using the method to inhibit or prevent inhibitory antibodies against the protein being provided via gene therapy, wherein the protein is encoded by a heterologous nucleotide sequence that is from the same species as said mammal.

However, at the time the invention was made, hemophilia mammals that do not produce factor VIII or Factor IX, but produce anti-factor VIII or anti-factor IX antibodies after exogenous administration of factor VIII or IX were well known to one of ordinary skill in the art as exemplified by Conti-Fine (columns 3-6 and 15). Conti-Fine further teaches one of ordinary skill in the art would want to use an immunosuppressive agent in combination with gene therapy to inhibit antibodies against the protein(s) because the protein or viral proteins are foreign to the subject and the subject would develop an immune response to these proteins (columns 6-7). Conti-Fine teaches a method of inhibiting or preventing inhibitory antibodies to Factor IX in a subject (e.g., humans) comprising administering an immunosuppressive agent, wherein the Factor IX is delivered via gene therapy to the subject (abstract and columns 3-7, 14-15, and 30). The gene therapy to the subject (e.g., human) comprising administering viral vector comprising Factor IX being from the same species as the subject (columns 4-6 and 14-15). The viral vector can be an adeno associated viral vector (columns 6, 15, and 27).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use a gene encoding a protein from the same species as the species being treated in the method. One

of ordinary skill in the art would have been motivated to combine the teaching for a reasonable expectation that the protein derived from the same species treated would have similar properties. See Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use a gene encoding a coagulation protein (e.g., Factor IX or Factor VIII) in the method. One of ordinary skill in the art would have been motivated to combine the teaching to treat hemophilia.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use either cyclophosphamide or anti-CD40 ligand to prevent inhibitory antibodies to the blood coagulation protein or use cyclophosphamide to inhibit inhibitory antibodies to the blood coagulation protein. One of ordinary skill in the art would have been motivated to combine the teaching to inhibit or prevent inhibitory antibodies against the protein being expressed via gene therapy because an immune response can be from expression of a protein (e.g., Factor IX) that is foreign to the host.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use an adeno associated viral vector in the method. One of ordinary skill in the art would have been motivated to combine the teaching for long-term expression of the protein.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use

the method in humans. One of ordinary skill in the art would have been motivated to combine the teaching for prolong expression of the protein in humans.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Wilson taken with Conti-Fine, namely to use a mammal having no detectable endogenous expression of the coagulation protein delivered in the method. One of ordinary skill in the art would have been motivated to combine the teaching to treat the mammal that does not express a coagulation protein (e.g., mammal with hemophilia A or B).

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments with respect to claims 1-4, 6-8, 10, 12-21, 23-25, 28, 29, and 31-41 have been considered but are moot in view of the new ground(s) of rejection.

Response to Arguments

Applicant's arguments, see page 8, filed 1/27/06, with respect to 112 second paragraph have been fully considered and are persuasive. The rejection of claims 1, 2, 4, 10, 24, and 28 has been withdrawn because the method does not omit an essential step required for gene therapy because the method can be performed before the gene therapy is carried out.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Crystal (US 20030134815). Crystal teaches, at the time the invention was made, that

one of ordinary skill in the art could delivery a viral vector comprising a gene to an individual (mammal, including humans), when the gene coding the therapeutic protein is derived from the species being treated. See page 3.

With respect to the 103(a), MPEP 2145 (II) recites: "Granting a patent on the discovery of an unknown but inherent function... "would re-move from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art." 596 F.2d at 1022, 201 USPQ at 661." The combination of Wilson, Crystal and Conti-Fine teach using one of ordinary skill in the art to use the same material(s) and method step(s) as recited in the instant claims. Thus, inhibiting or preventing inhibitory antibodies against the protein being expressed via gene therapy would flow naturally from the combination of Wilson, Crystal and Conti-Fine. See also Lantech Inc. v. Kaufman Co. of Ohio Inc., 878 F.2d 1446, 12 USPQ2d 1076, 1077 (Fed. Cir. 1989), cert. denied, 493 U.S. 1058 (1990).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, acting SPE – Art Unit 1635, can be reached at (571) 272-0811.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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BRIAN WHITEMAN
PATENT EXAMINER